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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/503,421	02/14/2000	Wilhelm Schwaeble	3523 P 004	6579

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EXAMINER	
ROMEO, DAVID S	
ART UNIT	PAPER NUMBER
1647	18

DATE MAILED: 06/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/503,421	Applicant(s) SCHWAEBLE	
	Examiner David S Romeo	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 April 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15 and 22-24* is/are pending in the application.

4a) Of the above claim(s) *1-9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-15 and 22-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-15 and 22-24* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The amendment filed April 1, 2003 (Paper No. 17) has been entered. Claims 1-15, 22-24 are pending. Claims 1-9 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Election was made without traverse in Paper No. 8. 1. Applicant elected without traverse group III, claim 10, to the extent that it is drawn to a method of treatment using a cC1qR binding domain, in Paper No. 8. Claims 10-15, 22-24 are being examined to the extent that they are drawn to a method of treatment using a cC1qR binding domain.

Maintained Formal Matters, Objections, and/or Rejections:

Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Krumdieck (a9) in view of Stuart (1996, cited by Applicants).

In addition, the examiner relies upon McCauliffe (u18) and Mazzarella (u9).

The rejection of record is applied to claims 11-15, 22-24.

The grounds of this rejection are of record.

In addition, Stuart discloses that the C1qR/CaR S-domain comprises amino acid residues 160-283 of C1qR/CaR (Table 1) and that the sequence of CaR is identical to the previously published CaR sequence of McCauliffe (McCauliffe et al. Molecular cloning, expression, and chromosome 19 localization of a human Ro/SS-A autoantigen. J Clin Invest. 1990 May;85(5):1379-91. PMID: 2332496) (page 246, left column, full paragraph 5). The CaR sequence of McCauliffe comprises SEQ ID NO: 1 of the present application, as indicated below:

```
A37047
calreticulin precursor - human
N;Alternate names: 52K ribonucleoprotein autoantigen Ro/SS-A; 60K integrin-binding protein; granule-associated 60-kD protein
C;Species: Homo sapiens (man)
C;Date: 10-Sep-1999 #sequence_revision 10-Sep-1999 #text_change 18-Feb-2000
C;Accession: A42330; A37047; A46452; A28812; PH1525; A40346; S11475; T45075
```

R;McCauliffe, D.P.; Yang, Y.S.; Wilson, J.; Sontheimer, R.D.; Capra, J.D.
J. Biol. Chem. 267, 2557-2562, 1992
A;Title: The 5'-flanking region of the human calreticulin gene shares homology with the human GRP78, GRP94, and protein disulfide isomerase promoters.
A;Reference number: A42330; MUID:92129342
A;Accession: A42330
A;Molecule type: DNA
A;Residues: 1-417 <MC2>
A;Note: sequence extracted from NCBI backbone (NCBIN:78537, NCBIP:78536)
R;McCauliffe, D.P.; Lux, F.A.; Lieu, T.S.; Sanz, I.; Hanke, J.; Newkirk, M.M.; Bachinski, L.L.; Itoh, Y.; Siciliano, M.J.; Reichlin, M.; Sontheimer, R.D.; Capra, J.D.
J. Clin. Invest. 85, 1379-1391, 1990
A;Title: Molecular cloning, expression, and chromosome 19 localization of a human Ro/SS-A autoantigen.
A;Reference number: A37047; MUID:90237213
A;Accession: A37047
A;Molecule type: mRNA
A;Residues: 1-417 <MCC>
A;Cross-references: GB:M32294; NID:g337486; PIDN:AAA36582.1; PID:g337487
A;Note: the authors translated the codon GTA for residue 349 as Tyr
R;Rokeach, L.A.; Haselby, J.A.; Meilof, J.F.; Smeenk, R.J.; Unnasch, T.R.; Greene, B.M.; Hoch, S.O.
J. Immunol. 147, 3031-3039, 1991
A;Title: Characterization of the autoantigen calreticulin.
A;Reference number: A46452; MUID:92013129
A;Accession: A46452
A;Molecule type: mRNA
A;Residues: 1-417 <ROK>
A;Cross-references: GB:M84739; NID:g179881; PIDN:AAA51916.1; PID:g179882
A;Note: sequence extracted from NCBI backbone (NCBIN:60749, NCBIP:60750)
R;Lieu, T.S.; Newkirk, M.M.; Capra, J.D.; Sontheimer, R.D.
J. Clin. Invest. 82, 96-101, 1988
A;Title: Molecular characterization of human Ro/SS-A antigen. Amino terminal sequence of the protein moiety of human Ro/SS-A antigen and immunological activity of a corresponding synthetic peptide.
A;Reference number: A28812; MUID:88273610
A;Accession: A28812
A;Molecule type: protein
A;Residues: 18-41 <LIE>
A;Note: 18-Ala was also found
R;Dupuis, M.; Schaerer, E.; Krause, K.H.; Tschopp, J.
J. Exp. Med. 177, 1-7, 1993
A;Title: The calcium-binding protein calreticulin is a major constituent of lytic granules in cytolytic T lymphocytes.
A;Reference number: PH1525; MUID:93115648
A;Accession: PH1525
A;Molecule type: protein
A;Residues: 18-27 <DUP>
A;Experimental source: LAK cell
R;Rojiani, M.V.; Finlay, B.B.; Gray, V.; Dedhar, S.
Biochemistry 30, 9859-9866, 1991
A;Title: In vitro interaction of a polypeptide homologous to human Ro/SS-A antigen (calreticulin) with a highly conserved amino acid sequence in the cytoplasmic domain of integrin alpha subunits.
A;Reference number: A40346; MUID:92002034
A;Accession: A40346
A;Molecule type: protein
A;Residues: 18-34,'R' <ROJ>
R;Krause, K.H.; Simmerman, H.K.B.; Jones, L.R.; Campbell, K.P.
Biochem. J. 270, 545-548, 1990
A;Title: Sequence similarity of calreticulin with a Ca(2+)-binding protein that co-purifies with an Ins(1,4,5)P(3)-sensitive Ca(2+) store in HL-60 cells.
A;Reference number: S11475; MUID:90380058
A;Accession: S11475
A;Molecule type: protein
A;Residues: 18-32 <KRA>
R;Lamerdin, J.; McCready, P.; Stilwagen, S.; Ramirez, M.; Carrano, A.
submitted to the EMBL Data Library, November 1996
A;Description: Characterization by genomic sequence analysis of a gene-rich 111 kb region of 19p13.2 containing the human DNA repair gene, RAD23A.
A;Reference number: Z22906
A;Accession: T45075
A;Status: preliminary; translated from GB/EMBL/DDBJ
A;Molecule type: DNA
A;Residues: 1-417 <LAM>
A;Cross-references: EMBL:AD000092; PIDN:AAB51176.1
A;Experimental source: cell line 5HL2-B; fibroblast
C;Comment: Autoantibodies specific for this protein are found in Sjogren's syndrome and several systemic lupus erythematosus-related disorders.
C;Genetics:
A;Gene: GDB:CALR
A;Cross-references: GDB:125179; OMIM:109091
A;Map position: 19p13.3-19p13.2
A;Introns: 31/1; 65/1; 133/1; 164/3; 234/3; 272/3; 320/3; 351/3
A;Note: CRTC
C;Superfamily: calreticulin
C;Keywords: calcium binding; integrin binding
F;1-17/Domain: signal sequence #status predicted <SIG>
F;18-417/Product: calreticulin #status predicted <MAT>
F;414-417/Region: endoplasmic reticulum retention signal

```
  Query Match           100.0%;  Score 702;  DB 1;  Length 417;
  Best Local Similarity  100.0%;  Pred. No. 1.3e-52;
  Matches  122;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy       1 RCKDDEFTHLYTLIVRPDNTYEVKIDNSQVESGSLEDDWDFLPPKKIKDPDASKPEDWDE 60
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     162 RCKDDEFTHLYTLIVRPDNTYEVKIDNSQVESGSLEDDWDFLPPKKIKDPDASKPEDWDE 221

Qy      61 RAKIDDPTDSKPEDWDKPEHIPDPDAKKPEDWDEEMDGEWEPPVIQNPEYKGEWKPRQID 120
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     222 RAKIDDPTDSKPEDWDKPEHIPDPDAKKPEDWDEEMDGEWEPPVIQNPEYKGEWKPRQID 281

Qy     121 NP 122
           ||
Db     282 NP 283
```

The high conservation of structure implies conservation of function and the corresponding region of mouse calreticulin differs by a single conservative amino acid substitution with respect to SEQ ID NO: 1, as indicated below (see also Mazzarella):

```
S06763
calreticulin precursor - mouse
N;Alternate names: 55K calcium-binding reticuloplasmin; calregulin
C;Species: Mus musculus (house mouse)
C;Date: 10-Sep-1999 #sequence_revision 10-Sep-1999 #text_change 10-Sep-1999
C;Accession: S06763; JC1444; PC1233; A57498
R;Smith, M.J.; Koch, G.L.E.
EMBO J. 8, 3581-3586, 1989
A;Title: Multiple zones in the sequence of calreticulin (CRP55, calregulin, HACBP), a major calcium binding ER/SR protein.
A;Reference number: S06763; MUID:90059955
A;Accession: S06763
A;Molecule type: DNA
A;Residues: 1-416 <SMI>
A;Cross-references: EMBL:X14926; NID:g50567; PIDN:CAA33053.1; PID:g50568
R;Mazzarella, R.A.; Gold, P.; Cunningham, M.; Green, M.
Gene 120, 217-225, 1992
A;Title: Determination of the sequence of an expressible cDNA clone encoding ERp60/calregulin by the use of a novel nested set
method.
A;Reference number: JC1444; MUID:93013037
A;Accession: JC1444
A;Molecule type: mRNA
A;Residues: 1-416 <MAZ>
A;Cross-references: GB:M92988; NID:g193084; PIDN:AAA37569.1; PID:g193085
A;Accession: PC1233
A;Molecule type: protein
A;Residues: 18-41 <MA2>
R;White, T.K.; Zhu, Q.; Tanzer, M.L.
J. Biol. Chem. 270, 15926-15929, 1995
A;Title: Cell surface calreticulin is a putative mannoside lectin which triggers mouse melanoma cell spreading.
A;Reference number: A57498; MUID:95332280
A;Accession: A57498
A;Status: preliminary
A;Molecule type: protein
A;Residues: 74-80;142-151;186-193 <WHI>
C;Superfamily: calreticulin
C;Keywords: calcium binding
F;1-17/Domain: signal sequence #status predicted <SIG>
F;18-416/Product: calregulin #status experimental <MAT>
F;413-416/Region: endoplasmic reticulum retention signal


  Query Match             99.6%;  Score 699;  DB 1;  Length 416;
  Best Local Similarity   99.2%;  Pred. No. 2.3e-52;
  Matches  121;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;

Qy       1 RCKDDEFTHLYTLIVRPDNTYEVKIDNSQVESGSLEDDWDFLPPKKIKDPDASKPEDWDE 60
           ||||||||||||||||||||||||||||||||||||||||||||||||||:|||||||
Db     162 RCKDDEFTHLYTLIVRPDNTYEVKIDNSQVESGSLEDDWDFLPPKKIKDPDAAKPEDWDE 221

Qy      61 RAKIDDPTDSKPEDWDKPEHIPDPDAKKPEDWDEEMDGEWEPPVIQNPEYKGEWKPRQID 120
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     222 RAKIDDPTDSKPEDWDKPEHIPDPDAKKPEDWDEEMDGEWEPPVIQNPEYKGEWKPRQID 281

Qy     121 NP 122
           ||
Db     282 NP 283.
```

It is further noted that the corresponding region of mouse calreticulin is identical to the amino acid sequence of SEQ ID NO: 3, as indicated below (see also Mazzarella):

```
S06763
calreticulin precursor - mouse
N;Alternate names: 55K calcium-binding reticuloplasmin; calregulin
C;Species: Mus musculus (house mouse)
C;Date: 10-Sep-1999 #sequence_revision 10-Sep-1999 #text_change 10-Sep-1999
C;Accession: S06763; JC1444; PC1233; A57498
R;Smith, M.J.; Koch, G.L.E.
EMBO J. 8, 3581-3586, 1989
A;Title: Multiple zones in the sequence of calreticulin (CRP55, calregulin, HACBP), a major calcium binding ER/SR protein.
A;Reference number: S06763; MUID:90059955
A;Accession: S06763
A;Molecule type: DNA
A;Residues: 1-416 <SMI>
A;Cross-references: EMBL:X14926; NID:g50567; PIDN:CAA33053.1; PID:g50568
R;Mazzarella, R.A.; Gold, P.; Cunningham, M.; Green, M.
Gene 120, 217-225, 1992
A;Title: Determination of the sequence of an expressible cDNA clone encoding ERp60/calregulin by the use of a novel nested set method.
```

```
A;Reference number: JC1444; MUID:93013037
A;Accession: JC1444
A;Molecule type: mRNA
A;Residues: 1-416 <MAZ>
A;Cross-references: GB:M92988; NID:g193084; PIDN:AAA37569.1; PID:g193085
A;Accession: PC1233
A;Molecule type: protein
A;Residues: 18-41 <MA2>
R;White, T.K.; Zhu, Q.; Tanzer, M.L.
J. Biol. Chem. 270, 15926-15929, 1995
A;Title: Cell surface calreticulin is a putative mannoside lectin which triggers mouse melanoma cell spreading.
A;Reference number: A57498; MUID:95332280
A;Accession: A57498
A;Status: preliminary
A;Molecule type: protein
A;Residues: 74-80;142-151;186-193 <WHI>
C;Superfamily: calreticulin
C;Keywords: calcium binding
F;1-17/Domain: signal sequence #status predicted <SIG>
F;18-416/Product: calregulin #status experimental <MAT>
F;413-416/Region: endoplasmic reticulum retention signal

  Query Match           100.0%;  Score 702;  DB 1;  Length 416;
  Best Local Similarity  100.0%;  Pred. No. 7.4e-53;
  Matches  122;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      1 RCKDDEFTHLYTLIVRPDNTYEVKIDNSQVESGSLEDDWDFLPPKKIKDPDAAKPEDWDE-60
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    162 RCKDDEFTHLYTLIVRPDNTYEVKIDNSQVESGSLEDDWDFLPPKKIKDPDAAKPEDWDE 221

Qy     61 RAKIDDPTDSKPEDWDKPEHIPDPDAKKPEDWDEEMDGEWEPPVIQNPEYKGEWKPRQID 120
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    222 RAKIDDPTDSKPEDWDKPEHIPDPDAKKPEDWDEEMDGEWEPPVIQNPEYKGEWKPRQID 281

Qy    121 NP 122
          ||
Db    282 NP 283.
```

It would have been further obvious to one of ordinary skill in the art at the time of Applicants' invention to use the region of mouse calreticulin that is identical to the amino acid sequence of SEQ ID NO: 3 and that the corresponds to the C1qR/CaR S-domain, with a reasonable expectation of success. One of ordinary skill in the art would be motivated to make this modification because one of ordinary skill in the art would have a reasonable expectation that the region of mouse calreticulin that corresponds to the C1qR/CaR S-domain binds to C1q and suppresses or inhibits C1 complex biological activity and will thereby suppress one or more of the deleterious effects of antibody-mediated complement activation, such as recruitment and activation of inflammatory cells, vasodilation, and/or direct cell killing via formation of membrane attack complex which is the lytic component system, thereby providing significant advantages over existing therapies and an ideal solution to the problem of complement activation.

Stuart's discloses that that strong C1q inhibitory activity is localized to the C1qR/CaR S-domain is consistent with the isolated C1qR/CaR S-domain being an antagonist of C1qR/CaR, i.e., "an inhibitor of the cC1qR binding domain."

The limitation "for binding a ligand to inhibit complement activation" is an intended use of the claimed method. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963).

Krumdieck discloses that substances that bind to C1q and suppress or inhibit C1 complex biological activity will suppress one or more of the deleterious effects of antibody-mediated complement activation, such as recruitment and activation of inflammatory cells. Stuart discloses that the C1qR/CaR S-domain is binds and inhibits C1q. Therefore, one of ordinary skill in the art would have a reasonable expectation that "inhibiting complement activation involved in the initiation and maintenance of inflammation" would naturally flow from following the teachings of the prior art.

Furthermore, in Figure 1 of the present application the CUB domain is underlined. See Figure 1 and page 5, full paragraph 1. No difference is seen between amino acid residues 160-283 of C1qR/CaR and the CUB domain shown in Figure 1. Accordingly, the method of treatment taught by the prior art "includes administering a complement ubiquitin (CUB) domain." Administration of the C1qR/CaR S-domain is "to be effective on complement ubiquitin (CUB) domain functionality" because there is no difference between amino acid residues 160-283 of C1qR/CaR and a cC1qR binding domain having the sequence of SEQ ID NO: 1 and a chemical composition and its properties are inseparable. An amount of the

C1qR/CaR S-domain effective to suppress or inhibit C1 complex biological activity and thereby suppress one or more of the deleterious effects of antibody-mediated complement activation, such as recruitment and activation of inflammatory cells, vasodilation, and/or direct cell killing via formation of membrane attack complex which is the lytic component system is "a therapeutically effective quantity of a complement ubiquitin (CUB) domain" or "a therapeutically effective quantity of a cC1qR binding domain useful in the treatment and maintenance of inflammation," in the absence of evidence to the contrary.

The invention is prima facie obvious over the prior art.

Applicants argue that the combination of references is improper because the cited prior art references do not suggest combining or modifying the references, that there must be some reason, suggestion , or motivation that would make the combination feasible, that there is no suggestion to combine the references. Applicants arguments have been fully considered but they are not persuasive. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Krumdieck teaches that substances that bind to C1q and suppress or inhibit C1 complex biological activity will suppress one or more of the deleterious effects of antibody-mediated complement activation, such as recruitment and activation of inflammatory cells, vasodilation, and/or direct cell killing via formation of membrane attack complex which is

the lytic component system, thereby providing significant advantages over existing therapies and an ideal solution to the problem of complement activation (see column 2, lines 25-38) and Stuart teaches that the S-domain of C1qR exhibits a strong inhibition of C1 formation (paragraph bridging pages 248-249). The teaching, suggestion, or motivation to combine the references comes from the reasonable expectation that the S-domain of C1qR will exert its expected function, i.e., strongly inhibit C1 formation, and achieve its expected result, i.e., suppress one or more of the deleterious effects of antibody-mediated complement activation, such as recruitment and activation of inflammatory cells, vasodilation, and/or direct cell killing via formation of membrane attack complex which is the lytic component system, thereby providing an ideal solution to the problem of complement activation.

In response to applicant's argument that there is no reason to modify the teachings of Krumdieck with that of Stuart, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). The teachings of the references would have suggested the combination to those of ordinary skill in the art. It is further noted that combining Krumdieck and Stuart does not change the principle of operation of Krumdieck nor does it render Krumdieck inoperable for its intended purpose.

Applicants argue that neither reference teaches that the C1q binding domain of C1qR is a CUB domain, that the references do not teach a medicament to effect or inhibit CUB domain functionality, and that Applicant has discovered that the C1q binding domain of cC1qR is in fact

a CUB domain, and thus previous unknown functionality can be attributed to cC1qR and inhibitors of same, and that certain functionality can be attributed to this CUB domain that is not taught by the cited references. Applicants arguments have been fully considered but they are not persuasive. Stuart teaches that the S-domain comprises amino acid residues 160-283 (Table 1). In Figure 1 of the present application the CUB domain is underlined. See Figure 1 and page 5, full paragraph 1. No difference is seen between amino acid residues 160-283 and the CUB domain shown in Figure 1. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise obvious invention.

Applicants argue that each of the references is teaching completely different concepts. Applicants arguments have been fully considered but they are not persuasive. Both Krumdieck and Stuart teach the same concept, which is the inhibition of C1.

Applicants argue that neither reference leads to any suggestion that by combining the teachings a better result would be accomplished. Applicants arguments have been fully considered but they are not persuasive. Stuart's teaching of strong inhibition of C1 formation by the S-domain of C1qR provides at least a reasonable expectation of that a beneficial result would be obtained by combining the teachings of Krumdieck and Stuart. Further, there does not appear to be a requirement that a better result be obtained.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

New formal matters, objections, and/or rejections:

Claim Rejections - 35 USC § 112

Claim 22 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to or encompass "an inhibitor of the cC1qR binding domain". The limitation "an inhibitor of the cC1qR binding domain" encompasses a genus of any and/or all compounds having the desired activity. The specification and claim do not indicate what distinguishing attributes shared by the members of the genus. The specification and claim do not place any limit on the structure of the genus. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Structural features that could distinguish compounds in the genus are missing from the disclosure. No common structural attributes identify the members of the genus. The claims do not even require that "an inhibitor of the cC1qR binding domain" be a protein. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NOs: 1-3 alone are insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Claim 22 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claim is directed to administering a cC1qR binding domain and an inhibitor of the cC1qR binding domain. Although the disclosure, as filed supports administering a cC1qR binding domain or an inhibitor of the cC1qR binding domain, it does not support administering a cC1qR binding domain and an inhibitor of the cC1qR binding domain, and the introduction of such a limitation raises the issue of new matter.

Claim 22 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NO: 1, SEQ ID NO: 2, or SEQ ID NO: 3, does not reasonably provide enablement for "an inhibitor of the cC1qR binding domain". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. The limitation "an inhibitor of the cC1qR binding domain" is analogous to a single means type of claim disparaged by the courts because the limitation encompasses every conceivable means for achieving the stated purpose whereas the specification discloses at most only those means known to the inventor. A single means claim, i.e., where a means recitation does not appear in combination with another recited element of means, is subject to an undue breadth rejection under 35 U.S.C. 112, first paragraph. In re Hyatt , 708 F.2d 712, 218 USPQ 195 (Fed. Cir. 1983) (A single means claim which covered every conceivable means for achieving the stated purpose was held

nonenabling for the scope of the claim because the specification disclosed at most only those means known to the inventor.). When claims depend on a recited property, a fact situation comparable to Hyatt is possible, where the claim covers every conceivable structure (means) for achieving the stated property (result) while the specification discloses at most only those known to the inventor.

The following claims are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 10-15, 22-24 are indefinite because they lack a process step which clearly relates back to the claim preamble and it is unclear what process is to be achieved; an intended use is not the same as achieving a result; in the absence of a recitation as to any result, or a process step producing a result, it is unclear what result of the process can be inferred. The metes and bounds are not clearly set forth.

Conclusion

No claims are allowable. SEQ ID NO: 2 is free of the prior art of record.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (703) 305-4050. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M.

IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, GARY KUNZ, CAN BE REACHED ON (703) 308-4623.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE FOLLOWING TC 1600 BEFORE AND AFTER FINAL RIGHTFAX NUMBERS:

BEFORE FINAL (703) 872-9306
AFTER FINAL (703) 872-9307

IN ADDITION TO THE OFFICIAL RIGHTFAX NUMBERS ABOVE, THE TC 1600 FAX CENTER HAS THE FOLLOWING OFFICIAL FAX NUMBERS: (703) 305-3592, (703) 308-4242 AND (703) 305-3014.

CUSTOMERS ARE ALSO ADVISED TO USE CERTIFICATE OF FACSIMILE PROCEDURES WHEN SUBMITTING A REPLY TO A NON-FINAL OR FINAL OFFICE ACTION BY FACSIMILE (SEE 37 CFR 1.6 AND 1.8).

FAXED DRAFT OR INFORMAL COMMUNICATIONS SHOULD BE DIRECTED TO THE EXAMINER AT (703) 308-0294.

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.

David Romeo

DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647

DSR
JUNE 26, 2003